

THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

Pituitary: **THE MASTER GLAND**

Special features
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A word from THE EDITOR...



With autumn upon us, we are pleased to bring you this pituitary-themed issue of *The Endocrinologist*. The Editorial Board had great fun thinking of titles for the issue – with pituitary analogies ranging from the conductor or controller to the nerve centre, which were mainly derived from our undergraduate teaching experiences! We finally settled on ‘Pituitary: the master gland’, inspired Dan Bernard, who uses this rather fitting terminology in his interview on page 9, which we hope you enjoy.

The feature articles encompass a breadth of basic science discoveries and veterinary and human pituitary-related medical advances. As a researcher into gonadotrophins, I was delighted to see George Bousfield’s article on page 6, discussing the importance of gonadotrophin hormone glycosylation, with an emphasis on the discoveries in the world of follicle-stimulating hormone (FSH) over the last 20–30 years. What he rather humbly omits is that he spearheaded many of the discoveries he describes. These include the ageing-dependent changes in FSH glycosylation, and how these impact FSH receptor engagement and downstream responses, some work that I have had the pleasure of contributing to.

It’s a real treat to have veterinary endocrinology featured in this issue. Rob Fowkes and Christopher Scudder describe comparative endocrine models on page 7. Who knew that some breeds of dog had a higher susceptibility to developing Cushing’s? And there are lessons learnt from an adrenocorticotropic-secreting pituitary tumour in a miniature schnauzer, no less! It’s a fascinating read, with the accompanying pictures really illustrating the recovery of the schnauzer post-hypophysectomy.

The summer conference round up covering the European Congress of Endocrinology and ENDO (page 26) reminds me that the Society for Endocrinology BES conference will soon be upon us. It looks like another great scientific line up, and I am looking forward to catching up with colleagues and friends. Who knows, perhaps I’ll even be on the winning team at the early career quiz night this year!

With best wishes

KIM JONAS

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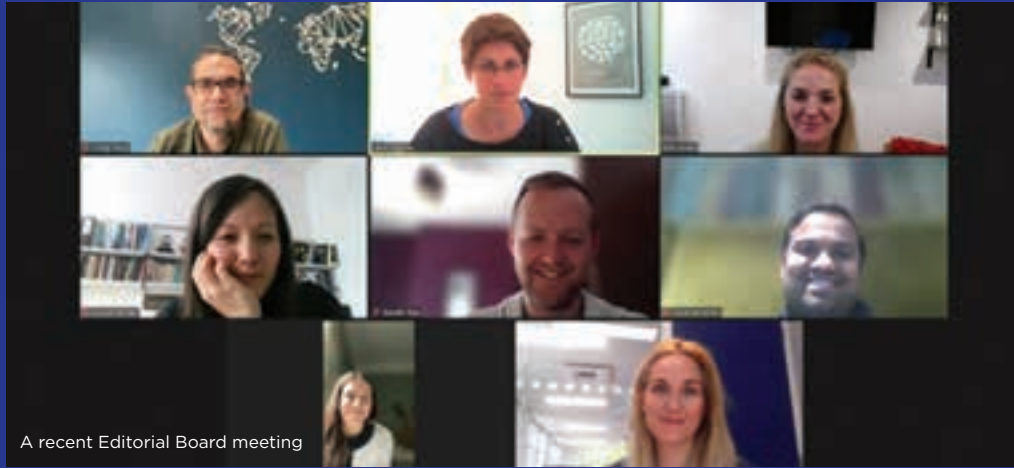
The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the WINTER 2023 issue: **5 October 2023**.

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JOIN THE ENDOCRINOLOGIST TEAM

We have vacancies on our Editorial Board! We want to hear from enthusiastic research scientists, clinicians and nurses, at any career stage, who have a passion for communicating endocrinology to our members. There's never been a more exciting time to join our team. Apply online by 4 October at www.endocrinology.org/editorialboard/apply.



A recent Editorial Board meeting

INSPIRE THE NEXT GENERATION AT Sfe BES 2023

Are you attending the Society for Endocrinology BES conference 2023? Why not take the opportunity to share your passion for endocrinology at our schools' outreach event on Wednesday 15 November? Local secondary schoolchildren will be invited to attend the conference on the final day, to learn more about the fascinating world of hormones and the experts making waves in our field. Find out how you can get involved at www.endocrinology.org/news/item/20055.



SERIES 3 OF OUR PODCAST IS HERE!

The latest series of our podcast, 'Hormones: The Inside Story', tackles health misinformation head on, busting myths around common hormonal conditions, and revealing some of the surprising ways that hormones impact all our lives. Champion endocrinology and share the podcast with your family, friends and colleagues! Now available on all major podcast platforms.

2023 STUDENT VIDEO AWARD

You can now watch the winning entries from our 2023 Student Video Award. Students were challenged to produce a short video, to engage the general public with endocrinology. The standard of submissions was very high once again. We congratulate this year's winners listed below.



1st place: Kisspeptin's promising role in treating hypoactive sexual desire disorder *Nina Supawaree & Ravi Patel (Imperial College London)* (pictured)

2nd place: Male hormonal contraception *Ryan Danvers (University of Edinburgh)*

3rd place: Understanding PCOS: science, symptoms and research *Alaina Shariff (University of Edinburgh)*

Find the winning videos at www.yourhormones.info/digital-library.

2023 LEADERSHIP AND DEVELOPMENT AWARDEES

The Society's Leadership and Development Awards Programme aims to recognise and nurture emerging talent, to enable our awardees to become the future leaders of endocrinology. Join us in congratulating our 2023 recipients:

Louise Hunter *University of Manchester*

Punith Kempgowda *University of Birmingham*

Edouard Mills *Imperial College London*

ESA-Sfe EXCHANGE AWARDEES

The ESA-Sfe Exchange Award fosters the development of collaborative international research projects by enabling members of the Endocrine Society of Australia (ESA) and the Society for Endocrinology to visit overseas researchers to initiate further studies. We congratulate our 2023 recipients:

Amy Dwyer *University of Adelaide*

Rayzel Fernandes *Imperial College London*



SOCIETY CALENDAR

21 September 2023
BITESIZE WEBINAR: USING TELEHEALTH FOR OUTPATIENT ENDOCRINE CARE
Online

3 October 2023
NATIONAL TRAINING SCHEME FOR THE USE OF RADIOIODINE IN BENIGN THYROID DISEASE
Birmingham, UK

3-4 October 2023
NATIONAL ENDOCRINOLOGY AND DIABETES TASTER SESSIONS
Online

13-15 November 2023
Sfe BES 2023
Glasgow, UK

www.endocrinology.org/events for full details



SOCIETY-ENDORSED EVENTS

27-28 September 2023
SIMBA REPRODUCTIVE ENDOCRINOLOGY AND PATIENT RELATED OUTCOMES
Birmingham, UK

30 September 2023
9TH BIRMINGHAM PITUITARY PRECEPTORSHIP INTERNATIONAL MEETING
Birmingham, UK

12 October 2023
WHAT'S NEW IN ENDOCRINOLOGY AND DIABETES 2023?
London, UK



GRANT AND PRIZE DEADLINES

20 September 2023
PUBLIC ENGAGEMENT GRANT

25 October 2023
PRACTICAL SKILLS GRANT

8 November 2023
EQUIPMENT GRANT

22 November 2023
MEETING SUPPORT GRANT

www.endocrinology.org/grants for full details of all Society grants and prizes

HOT TOPICS

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the Members' Area of the Society website, www.endocrinology.org. *Endocrine Connections*, *Endocrinology*, *Diabetes & Metabolism Case Reports* and *Endocrine Oncology* are open access and free to all. Publishing in *Endocrine Oncology* is currently free.



JOURNAL OF ENDOCRINOLOGY

Maternal androgens in early development: embryonic modification of a maternal effect

The effects of maternal testosterone on offspring traits and competitiveness in birds are widely studied. However, the fate of maternal testosterone during early embryonic development and its impact on offspring remain unclear. Wang *et al.* aimed to investigate two possibilities: either the rapid metabolism of maternal testosterone prevents it from reaching the embryos, leading to a potential conflict between the mother and offspring, or the metabolites facilitate the uptake of lipophilic testosterone from the yolk into the embryonic circulation, where they may function directly or convert back to testosterone.

To test their hypotheses, isotope-labelled testosterone (T-[D5]) was injected into freshly laid rock pigeon eggs. Analysis of the concentration and distribution of T-[D5] and its labelled metabolites in egg fractions at days 2, 5 and 10 of incubation was performed using liquid chromatography combined with tandem mass spectrometry.

Despite the use of a supraphysiological dosage of testosterone injection, a rapid decrease in yolk testosterone was observed within two days. It was metabolised into androstenedione, conjugated testosterone, etiocholanolone and components which were unidentified (due to methodological limitations). Interestingly, these findings demonstrate that testosterone, androstenedione and conjugated testosterone, but not etiocholanolone, reached the embryo, including its brain. Additionally, they found no sex-specific metabolism, which helps explain why maternal testosterone does not affect sexual differentiation.

Overall, this study provides novel evidence supporting both stated hypotheses. Maternal testosterone undergoes rapid conversion by the embryo, with several metabolites reaching the developing offspring. This research sheds light on the intricate dynamics of maternal-offspring interactions and the potential mechanisms underlying the effects of maternal testosterone on offspring traits.

Read the full article in *Journal of Endocrinology* **258** e220299



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JOURNAL OF MOLECULAR ENDOCRINOLOGY

CLEC11A improves insulin secretion and promotes human β -cell proliferation

Diabetes of all types is an ever-increasing problem worldwide. As a condition, it truly impacts every aspect of a patient's life, and there is growing pressure to find solutions to help curb the trend. Regardless of the specific type, a key hallmark of the disease is β -cell dysfunction, demonstrated by insufficient insulin release in response to hyperglycaemia. Much of the focus for research has been on slowing the decline or even reversing this dysfunction.

Shi *et al.* used a protein named C-type lectin domain containing 11A (CLEC11A), also known as stem cell growth factor, C-type lectin superfamily member 3 or osteolectin 1, to attempt to prevent β -cell dysfunction. This is a secreted sulfated glycoprotein that is highly expressed in bone marrow. Remarkably, not only is this protein expressed within both α - and β -cells of the pancreas, long term treatment with exogenous recombinant human

CLEC11A (rhCLEC11A) accentuated glucose-stimulated insulin secretion, insulin content and proliferation of human islet cells.

Using cell culture models and combined physiological testing, the group was able to demonstrate a 1.5-fold increase in islet content of insulin and improvement in the overall insulin content of close to 50%. Additionally, the group began to show some interesting links with levels of protein and levels of obesity, indicating a potential causal relationship between type 2 diabetes and obesity which may lead to a new way of thinking about the condition.

This could be the next new hope for those with diabetes and could potentially provide a novel therapeutic target for maintaining insulin production from within pancreatic β -cells in those with dysfunction. It is certainly a timely article which should be of interest to all endocrinologists.

Read the full article in *Journal of Molecular Endocrinology* **71** e220066

ENDOCRINE-RELATED CANCER

WHO classifications of pituitary neuroendocrine tumours: a clinico-pathological appraisal

Villa *et al.* review recent changes regarding pituitary gland tumours from both the 2021 *World Health Organization (WHO) Classification of Central Nervous System Tumours* (5th edition, CNS5) and the 2022 *WHO Classification of Endocrine and Neuroendocrine Tumours* (5th edition, ENDO5) in an informative way that is easy to digest.

Although concise, this review skilfully highlights the most relevant updates for those in the field, in an attempt to make the changes accessible to all who use them, avoiding the challenges seen in co-ordinating different books and text.

What is clear is the need to highlight the advancing role of molecular profiling and how this can enter into the classification of tumours. The authors are

mindful to reiterate that combined histological and molecular classification is yet to be fully established, but that relying solely on cell lineage has the potential to be too simplistic and can avoid reflecting the complexity of these tumours.

That the authors round off the piece by making their stance clear in terms of the need for standardisation should come as no surprise to those in the field. Ultimately, pathological, radiological, surgical and clinical reports must be brought together in concert before robust characteristic criteria can be fully created. This mini-review does, however, make some good progress in clearing the literature to allow for this standardisation to occur, and to establish reproducible pathways for risk stratification. The ultimate aim, of course, is to create better treatment for patients in terms of diagnosis and treatment.

Read the full article in *Endocrine-Related Cancer* **30** e230021

CLINICAL ENDOCRINOLOGY

Joint British Thyroid Association/Society for Endocrinology consensus statement on the use of liothyronine in hypothyroidism

The current disease burden of primary hypothyroidism is estimated to be around 3% of the population in the UK. Treatment is intended to return thyrotrophin (TSH) levels to the normal range and improve symptoms, and reduce the impact on quality of life.

The statement first discusses when and how levothyroxine (T4) monotherapy should be initiated. It provides a useful summary of conditions and situations in which TSH may remain elevated despite apparently adequate doses of T4 being prescribed.

Whilst T4 has been the general mainstay of treatment for hypothyroidism, there are subsets of patients who do not find symptomatic benefit from conventional

therapy. This statement discusses why this might be, and what additional/alternative treatment options are most commonly tried. Focusing on liothyronine (T3), it summarises where the current evidence base for T3 monotherapy and T3/T4 combination therapy stands.

This British Thyroid Association and Society for Endocrinology consensus statement outlines a recommended approach for supporting patients who wish to try T3 as a means of treating their hypothyroidism, centred around T3/T4 combination treatment. The recommendations do not advise T3 monotherapy except in the event of confirmed allergy to T4 or its excipients. The statement also provides advice on the practicalities of deprescribing T3 or desiccated thyroid extract. Variations in practice across the UK, and the need for more research in this area, are also highlighted.

Read the full article in *Clinical Endocrinology* doi:10.1111/cen.14935

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Recombinant human parathyroid hormone in pregnancy

Data are lacking regarding the use and safety of recombinant human parathyroid hormone 1–84 (rhPTH(1–84)) in pregnancy and breastfeeding. In light of the recent issues affecting rhPTH(1–84) availability for people with hypoparathyroidism, this may remain so for some time.

Here, Liao and Cusano report the case of a woman who acquired hypoparathyroidism following total thyroidectomy at the age of 28. Due to challenges in achieving stable serum calcium levels with calcium and calcitriol supplementation, she began rhPTH(1–84) therapy. Since commencing

rhPTH(1–84), she has had two pregnancies during which she continued rhPTH(1–84) in early pregnancy, as well as during breastfeeding.

The authors report the course of both pregnancies, including biochemistry and obstetric outcomes. They also summarise the changes that occur in calcium metabolism during pregnancy, and the current approaches to managing people with hypoparathyroidism in the antenatal and perinatal periods.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* doi: 10.1530/EDM-22-0401

ENDOCRINE CONNECTIONS

Trimethylamine oxide as a biomarker for diabetic kidney disease

In this study, Huang *et al.* reveal a novel association between serum trimethylamine oxide (TMAO) and diabetic kidney disease (DKD), indicating its potential as an independent risk factor for DKD. Significantly higher levels of TMAO were observed in patients with DKD compared with the control group and subjects with non-diabetic kidney disease. Previous research has linked gut microbiota-dependent TMAO to the development of type 2 diabetes mellitus (T2DM), with increased TMAO levels associated with insulin resistance and impaired glucose tolerance. However, this study did not find a statistically significant difference in serum TMAO levels between the group with diabetes and the control group, possibly due to the small sample size.

The study identified positive correlations between serum TMAO levels and blood urea nitrogen and serum creatinine levels, and a negative correlation with

estimated glomerular filtration rate, consistent with previous findings in patients with chronic renal failure. Multifactorial logistic regression analysis confirmed that increased serum TMAO levels independently contribute to the development of DKD. TMAO clearance by the kidneys may be disrupted in chronic kidney disease, potentially due to changes in gut microbial homeostasis and increased trimethylamine-producing bacteria.

In conclusion, this study establishes a link between elevated serum TMAO levels and the risk of DKD in patients with T2DM, highlighting TMAO as an independent risk factor for DKD development.

Read the full article in *Endocrine Connections* **12** e220542

ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.

Cardiovascular safety of testosterone replacement therapy

The issue of cardiovascular safety of testosterone replacement has been raised over the years, with both the US Food and Drug Administration and the European Medicines Agency previously determining that there was insufficient evidence to conclude whether testosterone therapy was associated with an increased risk of stroke or cardiovascular disease (CVD).

In this randomised, multicentre, double-blind, placebo-controlled, non-inferiority trial, Lincoff and colleagues enrolled over 5,000 male participants aged 45–80 with hypogonadism (defined as having 2x fasting testosterone values of <10.4nmol/l, and symptoms consistent with the condition), who were deemed to be at high risk of CVD. Participants were randomised at a 1:1 ratio to daily 1.62% daily testosterone gel or matched placebo.

Over a mean±SD duration of treatment of 21.7±14.1 months, with mean follow up of 33.0±12.1 months, testosterone replacement was non-inferior to placebo for major adverse cardiovascular events (MACE: testosterone group 182 patients (7.0%) versus placebo group 190 patients (7.3%)). Interestingly, there was a higher incidence of pulmonary embolism, acute kidney injury and atrial fibrillation in patients on testosterone replacement compared with placebo.

These data demonstrate that, even in men at high risk of CVD, transdermal testosterone replacement was non-inferior to placebo for major cardiovascular events.

Read the full article in *New England Journal of Medicine* **389** 107–117



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UNDERSTANDING GLYCOFORMS OF FOLLICLE-STIMULATING HORMONE

WRITTEN BY GEORGE R BOUSFIELD



Follicle-stimulating hormone (FSH) is a glycoprotein hormone that plays a central role in reproduction by regulating ovarian follicle granulosa cells and testicular Sertoli cells which express the FSH receptor (FSHR). Anterior pituitary glycoprotein hormones include FSH, luteinising hormone (LH) and thyroid-stimulating hormone (TSH). Primates and equids express a placental glycoprotein hormone, chorionic gonadotrophin (CG). These heterodimeric hormones possess a common α -subunit expressed by the *CGA* gene. Hormone-specific β -subunits, expressed by the *FSHB*, *LHB*, *TSHB* or *CGB* gene respectively, determine the identity of the heterodimer.

Both subunits are glycoproteins decorated with N-glycans at α Asn-52 and α Asn-78 in the α -subunit (the human hormone numbering will be used) and at one or two highly conserved β -subunit Asn residues. The latter differ in numbering due to N-terminal sequence length differences between β -subunits. N-Glycans are highly variable in structure because of a complex biosynthetic pathway that produces differences in glycan branch number and branch termination with negatively charged sialic acid or sulfate residues. Partial N-glycosylation occurs in β -subunits possessing two N-glycosylation sites. Variations in glycan structure and glycan number combine to produce isoforms, of which FSH isoforms have been most extensively studied.

THE IMPACT OF GLYCOSYLATION

The fact that glycoprotein hormone glycosylation is necessary for full activation of G_s by their cognate receptors has been known for over 40 years. While chemically deglycosylated LH receptor binding was not impaired, activation of the G_s -mediated cyclic AMP pathway was compromised.¹ Individual subunit deglycosylation revealed that α -subunit glycans exerted a greater impact on biological activity of the heterodimer than β -subunit glycans.¹ Site-directed mutagenesis of human CG (hCG) glycosylation sites confirmed the greater influence of α -subunit glycans, localised the critical oligosaccharide to α Asn-52, and revealed a complicated pattern of N-glycan influence on bioactivity.² Loss of any or all glycans other than that at α Asn-52 had no impact on biological activity. However, only partial loss of activity resulted from α Asn-52 glycan absence. Maximum activity loss required elimination of both α Asn-52 and β Asn-30 glycosylation sites.

Nevertheless, no naturally occurring isoforms exhibited loss of α Asn-52 glycans. Viktor Butnev proposed that the number or size of complex branches in α Asn-52 glycans correlated with biological activity based on studies with equine gonadotrophins: eLH, eFSH and eCG.³ As hCG α , hLH α and hFSH α Asn-52 glycans possess 1, 2 and 3 complex branches respectively, Wendy Walton set out to prepare hFSH α isoforms to test the branch number hypothesis. Along the way, she discovered naturally occurring hFSH variants lacking β -subunit glycans.⁴

β -SUBUNIT GLYCAN VARIATION

Western blots identify three FSH β bands at 18, 21 and 24kDa, which represent the lack of Asn-7 glycan, absence of Asn-24 glycan and presence of both glycans respectively. Protein sequencing revealed Asn residues at

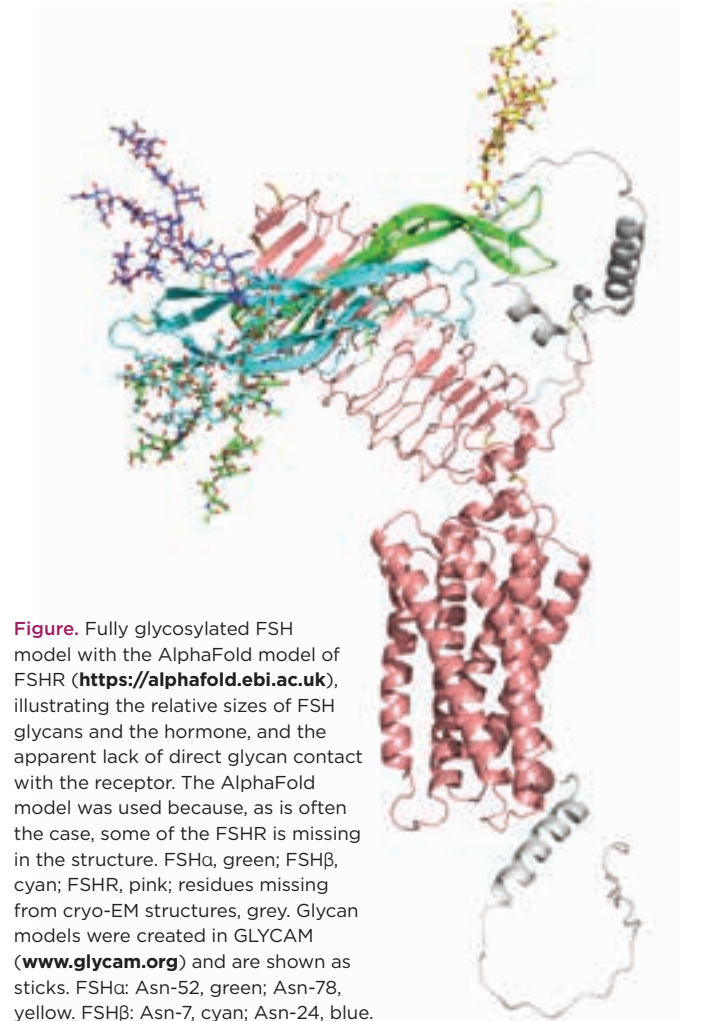


Figure. Fully glycosylated FSH model with the AlphaFold model of FSHR (<https://alphafold.ebi.ac.uk>), illustrating the relative sizes of FSH glycans and the hormone, and the apparent lack of direct glycan contact with the receptor. The AlphaFold model was used because, as is often the case, some of the FSHR is missing in the structure. FSH α , green; FSH β , cyan; FSHR, pink; residues missing from cryo-EM structures, grey. Glycan models were created in GLYCAM (www.glycam.org) and are shown as sticks. FSH α : Asn-52, green; Asn-78, yellow. FSH β : Asn-7, cyan; Asn-24, blue.

non-glycosylated sites, indicating oligosaccharyl transferase had skipped these sites. Mass spectrometry confirmed partially and fully glycosylated FSH β variants and revealed a non-glycosylated FSH β in human pituitary extracts. Thanks in large part to a FSH glycoform transgenic mouse model developed in Raj Kumar's laboratory, the three physiologically relevant FSH glycoforms (named after FSH β sizes) are FSH18, FSH21 and FSH24.⁵

An age-related switch from predominantly FSH21 to predominantly FSH24 occurs in female pituitaries. Partially and fully glycosylated FSH exhibit divergent patterns of serum concentrations during the menstrual cycle. FSH18 and FSH21 exhibit greater FSHR binding and biological activity than FSH24. The latter engages the receptor more slowly and occupies fewer receptors than preparations containing both FSH18 and FSH21.

Despite support for a trimeric FSHR model based on X-ray crystallography of the FSHR extracellular domain,⁶ hormone displacement studies suggest most FSHRs exist as monomers.⁷ PD-PALM studies in Kim Jonas' laboratory have revealed that 30% of the FSHRs are oligomerised, while FSH binding temporarily reduced this to 20%.⁸ FSH21/18 mixtures achieve this more rapidly than FSH24. A biased FSH agonist, devoid of cyclic AMP/protein kinase A activity, increases FSHR oligomerisation.

UNDERSTANDING RECEPTOR ACTIVATION

G protein-coupled receptor conformational flexibility challenges structural studies. The glycoprotein hormone receptors, including the FSHR, are no exceptions. X-ray crystallographic studies were limited to the FSHR extracellular domain (ECD) bound to deglycosylated FSH in order to obtain diffractable crystals.⁹ These studies defined protein–protein interactions involved in high affinity binding to the rigid ECD and interactions with the flexible hinge region.

Recent cryogenic electron microscopic (cryo-EM) reports describe largely complete structures for all three glycoprotein hormone receptors and reveal a common difference between the inactive and active conformations. The inactive receptor ECD is oriented downwards towards the membrane in the inactive state and rotated 38–48° upwards in the active, ligand-bound state.

Two different mechanisms for receptor activation have been proposed. The push–pull model, based on studies of all three receptors, proposes that when the ligand binds, a β -subunit steric clash with the membrane pushes the receptor ECD upwards from the down conformation and receptor hinge interactions with the ligand α -subunit pull the ECD to the fully up, active conformation.¹⁰

The glycan-propping model, based on studies of the TSH receptor, proposes that the ECDs flip back and forth between up and down positions.¹¹ ECD position alone is sufficient to activate or inactivate the receptor due to concomitant hinge conformational changes regulating transmembrane domain conformation. TSH binds the up conformation and stabilises it by steric clash of the α Asn-52 glycan with the membrane.

The same steric clash precludes glycosylated ligand binding when the receptor is in the down conformation.

Contributions by the β -subunit glycans to receptor binding and hormone activity are not explained by either model. As cryo-EM is compatible with glycosylated ligands, this technology may eventually provide mechanisms to explain the varying biological activities of glycoprotein hormone isoforms.

GEORGE R BOUSFIELD

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PITUITARY TUMOURS: A MENAGERIE OF MODELS

WRITTEN BY CHRISTOPHER J SCUDDER AND ROBERT C FOWKES



Pituitary tumours are among the most common forms of intracranial tumours in humans. Despite this, traditional models of pituitary disease have predominantly relied upon induced tumorigenesis in rodents or fish. These models can be genetically tractable, and have helped our understanding of candidate gene involvement in the development of pituitary tumours. However, a combination of their tightly controlled husbandry conditions and the lack of genetic diversity in their backgrounds has led to increasing interest in uncovering spontaneous models of disease – and the animal kingdom has not disappointed.

SPONTANEOUS TUMOURS IN OTHER ANIMALS

The spontaneous development of pituitary tumours has been identified in numerous animal species, including birds, cats, dogs, horses and monkeys. In some of these species, pituitary tumours are predominantly identified at necropsy. However, in others, active pituitary disease presents through a broad range of clinical signs that strongly phenocopy symptoms of human patients with pituitary tumours, such as poorly controlled type 2 diabetes mellitus, polydipsia, polyuria, hunger, seizures and impaired cognitive function.

The most common functional pituitary neuroendocrine tumours (PitNETS) treated by veterinarians are somatotrophinomas (over-secreting growth hormone) and corticotrophinomas (over-secreting adrenocorticotrophin

(ACTH)). These animal models of acromegaly (hypersomatotrophism) and Cushing's disease (hyperadrenocorticism) present in some companion animals more commonly than others. Cats develop acromegaly far more frequently than dogs, whereas pituitary-dependent Cushing's disease is the most common cause of cortisol excess in the dog population. These tumour types share similar features to those affecting humans, such as typically presenting as a local pituitary disease, and being challenging to medically manage. It turns out that our 'best friends' can help us understand even more about ourselves.

CANINE PITUITARY STUDIES

Dogs have provided some of the fundamental data that describe the link between the pituitary gland and metabolism. In the early 20th century,



Figure. Left: miniature schnauzer with an ACTH-secreting pituitary tumour. Note the poor coat condition due to too much cortisol. Middle and right: recovery post-hypophysectomy. ©Joe Fenn

Bernardo Houssay and colleagues used hypophysectomy (surgical removal of the pituitary gland) to reveal the influence of the pituitary on the function of peripheral endocrine organs (such as the adrenal, thyroid and pancreas). These studies ultimately led to a Nobel Prize in Physiology or Medicine in 1947.

Pathological descriptions of pituitary lesions in dogs were made throughout the 20th century, and included cases of pituitary dwarfism as well as functional pituitary tumours. Pituitary disease is relatively common in dogs, with pituitary abnormalities being present in approximately 26% of dogs at the time of death (including cysts, neoplasias, carcinomas and hypophysitis),¹ and ACTH-secreting pituitary tumours are the most common form of clinically relevant pituitary disease in dogs. So what, if anything, can they teach us?

INSIGHTS INTO GENETICS

Certain dog breeds are predisposed to Cushing's disease (e.g. bichon frisé, border terrier, miniature schnauzer),² and strong genetic susceptibility has been identified in breed lines, such as in a family of Dandie Dinmont terriers described in *Journal of Endocrinology*.³ As our understanding of the canine genome improves, we can take advantage of these spontaneous models of pituitary disease to better inform treatment plans, and also look at the aetiology of tumour susceptibility.

Indeed, recent whole exome sequencing studies have taken a comparative approach to identify novel candidate genes involved in Cushing's disease in humans and dogs, such as the transcriptional coactivator, *MAMLD1*.⁴ Furthermore, dogs with pituitary-dependent Cushing's were instrumental in confirming the role of the transcription factor *Tpit* in corticotroph development,⁵ as well as uncovering the importance of *Pax7* in mediating *Tpit*-induced differentiation of corticotrophs and melanotrophs.⁶ In common with human patients with Cushing's disease, canine corticotroph tumours express *PTTG1*, and the expression level is negatively associated with disease-free interval.⁷ Most recently, canine pituitary organoid cultures have been established from patients with Cushing's disease that provide a dynamic, 3D model system to perform techniques such as gene therapy and drug screenings, to enhance our understanding of corticotroph tumours.⁸

DIFFERENT CLINICAL APPROACHES

In many ways, the clinical manifestations of canine pituitary disease faithfully reproduce these endocrine disorders in the human population, and the major objective in treating these clinical signs is the reduction of cortisol. Here, treatment paradigms for dogs and humans with Cushing's disease differ – canine patients are medically treated to reduce adrenal production of cortisol, with drugs such as trilostane, mitotane and ketoconazole. Working via different mechanisms, these compounds

commonly reduce cortisol production, but do not deal with the pituitary tumour which can progress in size over time.

The most effective treatment of Cushing's disease in dogs is neurosurgery. At present, very few centres around the world (e.g. the Royal Veterinary College in London, UK, and centres in Utrecht in The Netherlands and Washington State in the USA) have surgeons and medical teams capable of performing hypophysectomy, and of managing the dogs post-operatively. This is quite remarkable, considering a similar surgical approach was first used over 100 years ago to demonstrate the role of the pituitary in canine metabolic function. We hope that, in due course, hypophysectomy will become a more accessible procedure for companion animals with pituitary disease, as long term survival rates for these surgically treated Cushing's patients can be up to five years.

In the UK alone, there are over 13 million dogs living with their accompanying humans, experiencing the same environmental exposures, and having lifestyles that often mimic our own (well, almost). Dogs undergoing hypophysectomy are typically treatment-naïve for pituitary-targeted management of their condition prior to surgery, so there is an opportunity for us to understand the cause of these tumours without interference from previous medical intervention. As we strive to better understand the debilitating effects of PitNETs in the human population, we would do well to look at companion animals to help us out. After all, there has never been a more relevant time to focus on a One Health approach to tackle globally relevant diseases.

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AN INTERVIEW WITH... DAN BERNARD

Professor Dan Bernard is Director of the Centre for the Study of Reproduction at McGill University, Montréal, Canada. Here, he shares his interesting research journey and career highlights with Editor of *The Endocrinologist*, Kim Jonas.

Please tell us about your main research area

We are principally interested in the endocrine and neuroendocrine control of reproduction. Our major areas of research concern signalling by gonadotrophin-releasing hormone (GnRH), activins and inhibins in pituitary gonadotrophs, and the control of follicle-stimulating hormone (FSH) and luteinising hormone (LH) synthesis.

How did your career bring you to this point?

It has been a long and circuitous journey, and I will try to keep the story as short as possible, though I suppose it might be a useful tale for early stage scientists about following your interests.

As an undergraduate, I conducted two years of independent research studying visual perception in birds. This led to my initial graduate work on auditory perception, again using avian models. However, during my first year of graduate school, I took a course in neurobiology and behaviour, and found myself particularly excited about the section on the neural control of birdsong. It turns out that songbirds have evolved structures (nuclei) in their brains that enable them to both learn and produce song. These regions are sexually dimorphic, as it is typically the males that sing. They are also highly plastic. The regions grow and shrink as singing waxes and wanes. Birds typically sing in the breeding season as their testosterone levels increase. The so-called 'song control nuclei' contain steroid receptors, including androgen receptors, and testosterone can drive increases in singing behaviour and volumes of brain nuclei.

Coincidentally, in my second year of graduate school, my department recruited a new investigator who was studying this system. I started a collaborative project between the two labs. By the start of my third year, it was clear to everyone where my interests lay, and I moved to the new lab where I completed my PhD. My research showed that it was the act of singing rather than testosterone that drove the increases in size of the brain nuclei. That is, testosterone made the birds more likely to sing. Singing in turn promoted changes in the brain. This was akin to a muscle growing in response to repeated use.

For my postdoc, I was encouraged to move to a mammalian system (if I wanted a job in academia). But I was still very much interested in brain plasticity. So, I decided to work on brain changes in seasonally breeding Siberian hamsters. In this species, long day lengths promote activity of the hypothalamic-pituitary-gonadal (HPG) axis. In contrast, the HPG axis is 'turned off' under short (winter-like) day lengths. We already knew that GnRH expression was not altered in the brains of these animals, so this suggested there was another mechanism mediating changes in reproductive physiology. We therefore decided to do a differential gene expression analysis of the hypothalami of short- and long-day hamsters. At the time, the methods were primitive by today's standards. We employed an approach called differential display, which was also known as differential display because of the high rate of false positives and negatives! This was my experience, and we really did not pull out anything interesting from the brains of these animals. However, we did note that when we moved hamsters from short to long days, FSH levels went up quickly while LH levels remained low. I became very interested in the differential regulation of FSH and LH. This led to a second postdoc where I focused on the

mechanism of inhibin action. Inhibins suppress FSH production by pituitary gonadotrophs. So, this is how I ended up 'in the pituitary' where I remain today.

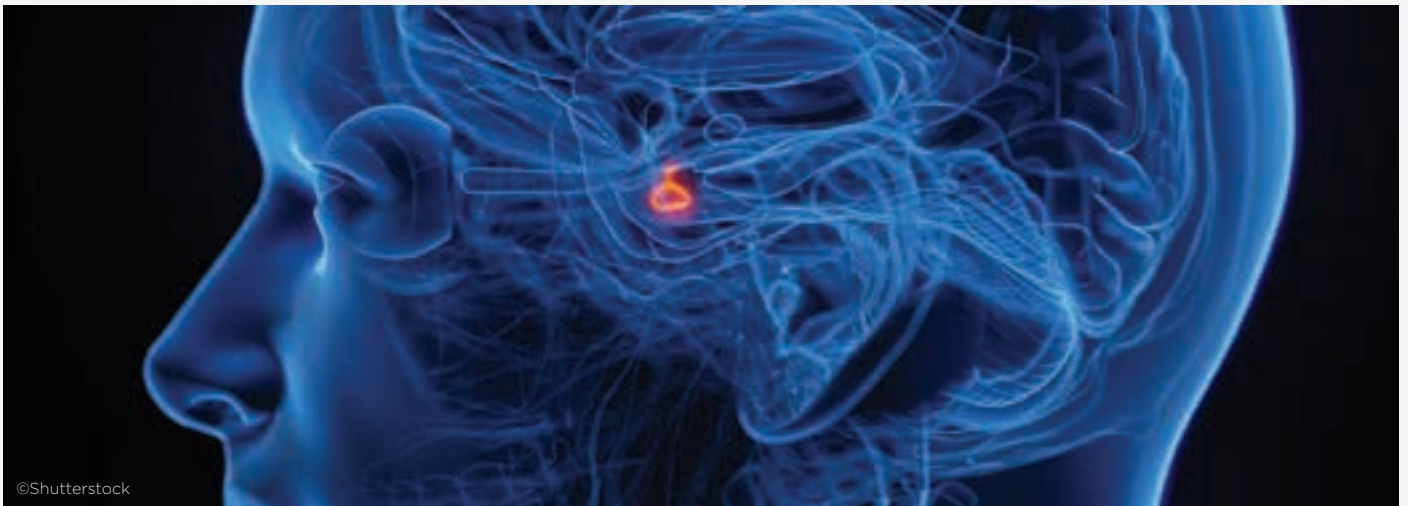
What has kept you interested in the pituitary for so long?

It's the master gland. Need I say more? In all seriousness, the pituitary is a very interesting tissue. The anterior lobe has five hormone-secreting cell types that control diverse aspects of physiology. My lab is interested in gonadotrophs (FSH and LH) and thyrotrophs (thyrotrophin; TSH).

With respect to gonadotrophs, there was a series of questions I wanted to answer. What transcription factors restrict FSH production to gonadotrophs? How do activins stimulate FSH production? How do inhibins suppress FSH production? In the almost 22 years I have been running a lab, I am happy to say we have answered many of these questions. But, as we all know, answers often inspire new questions, which continue to keep us busy.

Our work on thyrotrophs was a bit of a happy accident. In my second postdoc, I was working on a putative inhibin receptor. It turns out that this protein is not an inhibin receptor in gonadotrophs but rather regulates TSH production in thyrotrophs. Mutations in the gene encoding the protein are the most common cause of central hypothyroidism in people. We continue to investigate how this protein functions to regulate TSH synthesis and secretion.





How have advances such as the omics explosion shaped your research?

It is funny. When I first heard about single cell omics approaches, I did not immediately jump into using them. We are a question-driven rather than method-driven lab, and I just did not see how we needed these tools to answer any of our questions at the time. Well, I was wrong.

We knocked out the putative inhibin receptor in mice and did not get the expected effect. We realised that there must be another receptor but did not know how to identify it. Fortunately, right at that time, another group published the first single cell RNA-sequencing analysis of the mouse pituitary and a new gene popped up (one we had never heard of), which turned out to be exactly what we were looking for.

Since then, we have been very enthusiastic about these approaches and employ them frequently, thanks to vital collaborations with real experts in the field. Using single nucleus ATAC-seq, we identified enhancers for the FSH β gene that we would never have found without these amazing tools.

What have been your career highlights?

This is a tough one to answer. Personally, my most gratifying moments were earning my PhD, landing my first independent position, getting my first grant, and watching the maturation of my graduate students into scientists.

In terms of scientific discoveries, the top one so far has been the cloning of the inhibin B co-receptor, TGFBR3L. We have another exciting story that we have been working on for several years that should be published in the next year. Stay tuned...

And what are your top three publications (impact factor/citation index aside)?

This is like asking someone to pick their favourite child. I guess I would rather comment on three papers that may end up having the greatest impact long term. The first is our discovery, with our team of international collaborators, that mutations in *IGSF1* cause central hypothyroidism.¹ The second was our recent discovery of TGFBR3L as the inhibin B co-receptor.² This was only published in late 2021, but we think this could have impact in several areas, including in infertility treatment. Finally, there is our discovery that FOXL2 is a selective regulator of FSH synthesis in gonadotrophs.³ As I mentioned, we have a long-standing interest in differential regulation of the gonadotrophins. This was the first demonstration of a transcription factor that uniquely regulates FSH versus LH synthesis.

What papers have inspired you?

In the field, I think I have been most inspired by the first paper that identified betaglycan as an inhibin co-receptor.⁴ It inspired a lot of my work – as well as my gmail address and Twitter handle (@BetaglycanDan)!

I think the paper that affected me most as a scientist, however, was ‘Strong inference’ by John Platt.⁵ There are elements that are anachronistic today (it was published in 1964), but it is a blueprint for how to do science. It is a must-read for new graduate students in my opinion. I read it in my first year of graduate school and it still influences me today.

How have your research environment and collaboration shaped your research?

They have both been very important. We are all shaped by our environment. I have worked on things in my career that I never would have if not for my local colleagues. For example, the Montréal area has many investigators working on G protein-coupled receptors. We might have stuck to transforming growth factor- β family signalling and not looked at GnRH or gonadotrophin signalling if it had not been for the support and encouragement of colleagues.

Collaborations have been absolutely essential to any successes we have had. Collaboration is a win-win situation. When we lack expertise (which is often), we never hesitate to reach out to experts to ask for their help and collaboration. This has led to a lot of new discoveries and friends. We are also quick to help when others think we may be of assistance.

What advice would you give to trainees forging a career in research?

First, follow your interests. Secondly, never marry for money; move where the rich people are and marry for love. The point here is that you should work on what you are passionate about, and it is all the better if it is in a fundable area!

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ARTIFICIAL INTELLIGENCE IN PITUITARY SURGERY



WRITTEN BY OLIVER E BURTON, DANYAL Z KHAN AND HANI J MARCUS

Pituitary tumours are one of the most common types of intracranial tumour and account for up to 22.5% of all cases.¹ Artificial intelligence (AI) represents one of the most powerful tools in the modern neurosurgeon's arsenal in tackling these tumours. It constitutes a true paradigm shift in the way patients with pituitary tumours can be managed, not just on the operating table, but through the entirety of their journey.

PREOPERATIVE ISSUES

Diagnosing pituitary adenomas presents a perplexing challenge, due to the tumours' non-specific and subtle presentations. A single physician may not join the dots, and diagnostic delay – which can often be for many years – results in a tumour that is larger and harder to resect safely. The spread of tumours to critical areas, such as the cavernous sinus, represents a crucial factor affecting surgical outcomes, and even the most skilled neurosurgeon and their team may struggle to excise a tumour that could have been easily managed years earlier.

The wealth of patient data contained within medical records has the potential to unlock diagnostic solutions. However, the sheer volume of information generated from a single hospital visit overwhelms the capacity of a single clinician to process it swiftly. Enter large language models (LLMs), an exciting family of machine learning models that have been trained on vast amounts of textual data. Equipped with natural language processing capabilities, these AI models can swiftly analyse text, answer queries and categorise data, as well as perform their own variant of clinical reasoning.² Harnessing the power of LLMs enables medical teams to swiftly comb through a patient's complete medical history.³

Generative AI models can be used to raise suspicion of disease even in cases where patients are admitted under entirely different services. Weighting predictions based on health records, including blood tests and results of other investigations, may therefore allow clinicians to make the diagnosis of pituitary tumours years in advance of when they otherwise would, therefore reducing the tumour burden and improving the likelihood of successful management.⁴ This concept has already been demonstrated in other conditions affecting the brain, such as normal pressure hydrocephalus.⁵

OPERATIVE CONSIDERATIONS

Intraoperative neurosurgical decisions are often highly complex and made under pressure, which can lead to significant variation in practice. Data gathered both from the live surgical video and from devices worn and wielded by members of the operating team⁶ may allow the operating room of the future to 'orchestrate team members to a common workflow'.⁷ AI systems are already able to monitor the surgical field to detect different steps of each operation, watching for changes in instruments, the relevant anatomy, and the actions taken.⁸ In the first instance, this can drive efficiency by tracking progress during surgery and alerting team members during critical moments, automatically writing operative notes, and indexing cases for future teaching.

Most excitingly, this form of workflow analysis can also be used to explore the variations in operative practice, comparing the corresponding outcomes, and using this analysis to inform decision making in future cases. Using AI to analyse thousands of cases from international centres could offer each surgeon decision support when required, using the latest large scale

databases, and make suggestions based on past similar surgeries, or guide a surgeon in unknown territory.

POSTOPERATIVE FACTORS

Of course, resection is only part of the challenge. The patient must be monitored closely during their inpatient postoperative phase, and only sent home when it is safe to do so. Predicting short term patient outcomes after pituitary surgery is well known to be very difficult, with common complications including hypopituitarism, dysnatraemia and cerebrospinal fluid rhinorrhoea.⁹ Neural networks might be useful in stratifying patients into high and low risk groups through analysis of preoperative, operative and postoperative datasets, allowing some patients to be discharged early through rapid recovery protocols,¹⁰ and others to be kept longer for closer monitoring.

'Using AI to analyse thousands of cases could offer each surgeon decision support when required, and make suggestions based on past similar surgeries, or guide a surgeon in unknown territory.'

Moreover, on discharge, tumours that appear identical in pathology and postoperative imaging can exhibit vastly different behaviours in the long term, with some far more at risk of recurrence and the need for additional interventions, whether surgical or otherwise. A patient's journey represents a rich, multimodal and longitudinal dataset characterised by complex and non-linear relationships between variables. This intricacy provides a prime opportunity for AI solutions to piece together the puzzle and aid in expediting patients' discharge from hospital.

CONCLUSION

To close, AI is as much Pandora's box as panacea. The applications of large scale, big data analysis and autonomous learning are countless – but clinicians have a responsibility to their patients to use these tools carefully and responsibly. The future of pituitary surgery lies in the harmonious synergy between the surgeon and AI, transcending the limitations of each individual component, and neurosurgeons have a duty to embrace this paradigm shift for the betterment of both their craft and their patients.

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Although the condition might be rare...



...the features are common

Perhaps it's Cushing's syndrome, perhaps it's something else? If you connect any of these dots within a patient, consider referring them to a specialist endocrinologist.

For a clinician's guide to recognising Cushing's syndrome's signs and features, email cushings@connectthedots.health and help shine a light on this rare condition.



PITUITARY SURGERY SPECIALIST NURSE: A CAREER INSIGHT

WRITTEN BY FIONA CAINS



Fiona Cains tells us how she came to be a Pituitary Surgery Clinical Nurse Specialist, the challenges and rewards of the role, and what her job means for the patients she supports and their families.

MY JOURNEY SO FAR

My interest in the endocrine system began when I was a newly qualified staff nurse working on a diabetes and endocrinology ward. I looked after a patient who had type 1 diabetes and Addison's disease. I had no idea what Addison's disease was, so tasked myself with learning more about it, so that I could provide the best care for my patient. From then on, I was fascinated by the complexity and importance of hormones and actively pursued a role in endocrinology.

I subsequently joined the Christie Hospital in Manchester as a staff nurse on the Endocrine Unit and, in time, progressed to sister. I was privileged to work with and learn about endocrinology from the renowned and supportive endocrine team.

In my role, I carried out endocrine dynamic function tests, nurse-led clinics, visual fields tests and DXA (dual energy X-ray absorptiometry) scanning. I completed the paediatric endocrinology module at Keele University and the Royal Osteoporosis Society training scheme for bone densitometry. I was involved in the care of patients with a variety of endocrine conditions, including pituitary tumours and endocrine late effects of cancer treatments. This is where my interest in the pituitary gland really developed. A large part of my role was patient education and support. I regularly attended the regional pituitary multidisciplinary team (MDT) and neuroendocrine MDT meetings.

'The specialist nurse can identify issues or complications early, and initiate timely investigations and interventions. This can significantly improve patient outcomes.'

BECOMING A PITUITARY SURGERY SPECIALIST NURSE

In 2018, I joined the neurosurgery team at the Manchester Centre for Clinical Neurosciences in the newly created role of Pituitary Surgery Specialist Nurse. Manchester has one of the largest centres for pituitary surgery in the UK. The service manages the care of patients diagnosed with functioning and non-functioning pituitary neuroendocrine tumours, craniopharyngiomas, Rathke's cleft cysts, arachnoid cysts, and inflammatory and infective conditions.

My role is both supportive and clinical. I am involved in the care of patients attending the neurosurgery and joint neurosurgery–endocrine clinics, and provide information and support for patients and their families. Not all patients will proceed to surgery. Some patients are kept under radiological and endocrine surveillance. Some may have had previous surgery and are referred to oncology for radiotherapy.

Preoperative consultations with the specialist nurse are offered to all patients. The consultation focuses on answering patient's questions about their diagnosis, surgery and recovery. The majority of pituitary surgery is performed via a transsphenoidal approach, and in some cases a craniotomy may be required. Some patients may need shunts and other neurosurgical interventions.

The psychological impact of living with a pituitary condition and having surgery and other treatments can be very challenging for patients and their families. Establishing a good nurse–patient relationship prior to surgery is

A DAY IN THE LIFE OF A PITUITARY SURGERY SPECIALIST NURSE

- Carrying out preoperative consultations with patients to discuss diagnosis, aims and risks of surgery, managing patients' expectations, ensuring all appropriate investigations have been carried out prior to surgery
- Arranging radiology imaging and visual field/ophthalmology assessments
- Inpatient reviews
- Participation in pituitary multidisciplinary team (MDT) meetings
- Twice weekly nurse-led clinics (all postoperative patients are reviewed in this clinic at approximately one week after surgery). The clinics include:
 - visual assessments
 - assessment and investigations to diagnose/exclude disorders of water and sodium imbalance
 - diagnosis and treatment of infections
 - assessment for surgical complications
 - ensuring that patients have an appropriate postoperative plan in place for endocrine assessment, imaging, visual fields testing
 - MDT discussion, communication with respective endocrine teams
- Reviewing patients on the waiting list for surgery who report visual deterioration or other concerning symptoms
- Weekly attendance at endocrine investigation results meeting
- Production and updating of patient information
- Research and audit
- Provision of teaching sessions for nurses, students and healthcare professionals
- Liaising with physiotherapists/occupational therapists/neuropsychology/social care
- Provision of a buddy network for patients
- Liaising with the pituitary neurosurgeons, paediatric neurosurgery team and endocrinology team for children with surgical pituitary conditions
- Liaising with other specialist centres for complex quaternary referrals from other neurosurgical centres, including teenage and young adult patients

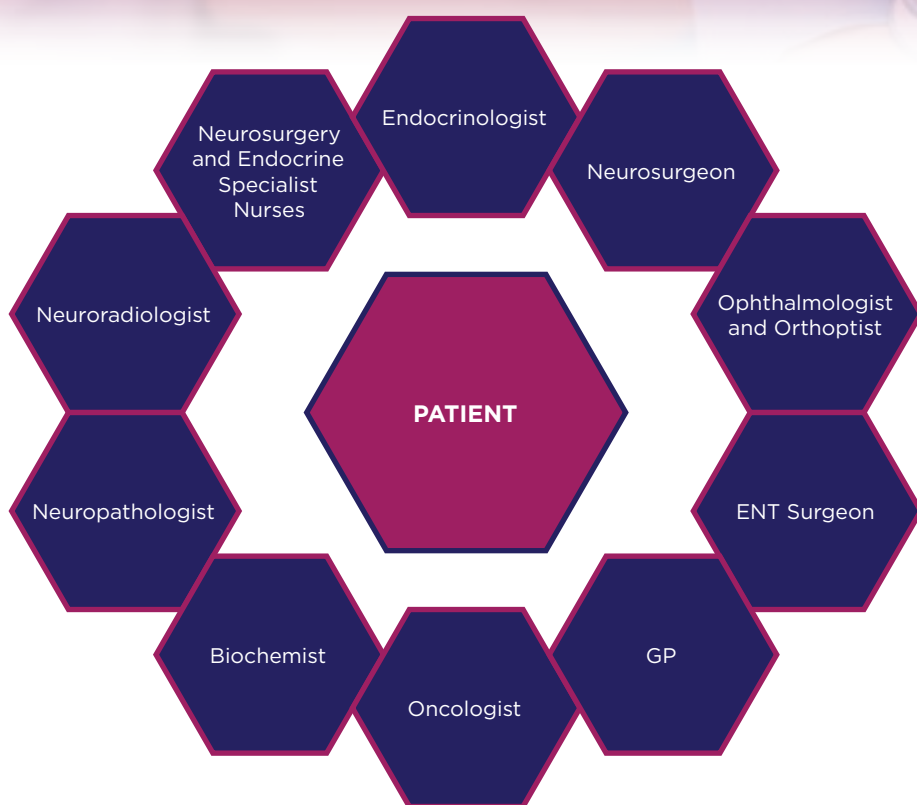


Figure. Management of patients with pituitary conditions involves a team of healthcare professionals.

beneficial in many ways. It builds continuity and patients are then more likely to seek support from me. Patients may need ongoing psychological support and input from a neuropsychologist and I can facilitate this.

The complexity of pituitary tumours and other pituitary disorders means that those patients who have surgery need a high level of input from the specialist nurse, and joint care between the neurosurgery and endocrine teams, during the pre- and postoperative phases. The specialist nurse can identify issues or complications early, and initiate timely investigations and interventions. This can significantly improve patient outcomes.

I am involved in the clinical management of postoperative inpatients, patients readmitted with complications such as syndrome of inappropriate antidiuretic hormone secretion (SIADH) and new acute patients presenting with apoplexy or a newly diagnosed pituitary condition. I review patients on a daily basis on the neurosurgery wards and critical care. The issues that I manage and give advice on include AVP deficiency (diabetes insipidus), SIADH and steroid management.

MAKING A DIFFERENCE

There has been a reduction in the number of avoidable hospital readmissions since my appointment, and a reduction in postoperative

complications. The length of inpatient hospital admissions has reduced. Prior to my appointment, pituitary patients requiring review would be assessed by a neurosurgery registrar in a neurosurgery ward clinic. Patients are now reviewed in the nurse-led clinic. The benefits of this include the easy access patients have to the clinic, continuity of care, the provision of expert clinical care, and a reduction in workload for the neurosurgery consultants and registrars.

CHALLENGES

The COVID-19 pandemic initially halted transsphenoidal pituitary surgery. Supporting patients who were waiting for surgery was challenging. Thankfully, we are performing surgery at our prepandemic level now. The main challenge for me has been transitioning from endocrine nurse to neurosurgery nurse. I have had excellent support and mentoring from the consultant neurosurgeons and the skull base specialist nurses. Other challenges are that, as a lone worker, workload management and personal development can be difficult. Current nursing shortages can mean that I need to spend more time on the wards managing patients' clinical care and educating new staff.

WHAT I FIND REWARDING

The most rewarding aspects of my role are positive patient outcomes after surgery: visual improvement for patients, and biochemical cure achievement for patients with functioning tumours. I particularly enjoy supporting patients with complex needs.

As a member of the Pituitary Foundation Medical Committee, I am passionate about sharing my knowledge of the pituitary gland and pituitary disorders with patients and healthcare professionals. My role as a member of the pituitary team provides a vital link between neurosurgery and endocrinology. Because of my previous endocrine nursing experience, I have strong links within endocrinology. These links enable good communication between healthcare professionals, which benefits the patient. Good communication and strong professional links are essential for the delivery of high quality patient care and the development of pituitary services.

I have always enjoyed being involved in delivering collaborative patient-centred care, and being part of a large specialist team, delivering expert care with colleagues who share my desire to provide the best care for pituitary patients.

FIONA CAINS

Pituitary Surgery Clinical Nurse Specialist, Manchester Centre for Clinical Neurosciences, Salford Royal Hospital, Northern Care Alliance

OXYTOCIN DEFICIENCY IN CENTRAL DIABETES INSIPIDUS (AVP DEFICIENCY)

WRITTEN BY CIHAN ATILA AND MIRJAM CHRIST-CRAIN



The hormone oxytocin is important for social interaction, is involved in emotion regulation and has anxiolytic properties. Researchers from the University Hospital of Basel (Switzerland) have succeeded in demonstrating a clinically relevant deficiency of oxytocin in patients with vasopressin deficiency (AVP deficiency or central diabetes insipidus). This finding could be key to developing new therapeutic approaches.

CURRENT UNDERSTANDING FROM RESEARCH

Even though the hormones oxytocin and vasopressin are both produced in the same hypothalamic area and are almost similar in structure, they have different functions in the body (Figure 1). Vasopressin is the main endocrine regulator of renal water excretion, and maintains fluid balance by keeping plasma volume and osmolality within narrow limits.¹ The main function of oxytocin is to promote prosocial effects such as in-group favouritism, trust and attachment. It increases empathy, improves emotion recognition and has anxiolytic effects.²

Disruption of the hypothalamic–pituitary area can cause a deficiency of vasopressin, known as central diabetes insipidus, which is clinically characterised by polyuria and polydipsia.¹ Despite treatment with desmopressin (a vasopressin receptor 2 agonist), patients often report residual psychological symptoms. The available studies in these patients have suggested heightened anxiety and difficulties describing or expressing emotions, reduced empathic abilities, higher levels of self-reported autistic traits, lower levels of joy when socialising, and lower scores in an emotion recognition task.^{3–6}

Due to the anatomical proximity, disruptions leading to vasopressin deficiency could also affect oxytocin-producing neurones. An additional oxytocin deficiency in these patients could explain – at least partially – the observed socio-emotional and psychological changes. Few studies have attempted to measure oxytocin in these patients, delivering inconclusive results.^{4,7} For other pituitary hormones, a provocation test is often applied in case of a suspected deficiency. So far, however, no standard provocation test for oxytocin has been established to prove this disease entity.

NOVEL OXYTOCIN PROVOCATION TEST

Methylenedioxymethamphetamine (MDMA, also known as ‘ecstasy’) is used recreationally for its effects on empathic feelings and sociability. Several studies have documented marked increases in circulating oxytocin levels in response to MDMA in healthy adults.^{8,9} The prosocial effects of MDMA on emotion processing and social interaction, such as increased trust, closeness to others, identification of facial emotions, and fear extinction, are mediated partly by a strong oxytocin release.⁹

Using MDMA (‘ecstasy’) as a psychoactive and biochemical provocation test, our recent study has, for the first time, indicated a clinically relevant oxytocin deficiency in patients with vasopressin deficiency.¹⁰ In healthy controls, there was an expected eightfold increase in plasma oxytocin from 77pg/ml (interquartile range (IQR) 59–94) at baseline by 659pg/ml (IQR 355–914) in response to MDMA stimulation, with

WHAT ARE OXYTOCIN AND VASOPRESSIN?

Oxytocin and vasopressin are both neuropeptides and hormones produced from the hypothalamus and released by the posterior pituitary, with roles classically associated with reproduction, water homeostasis and social behaviours.

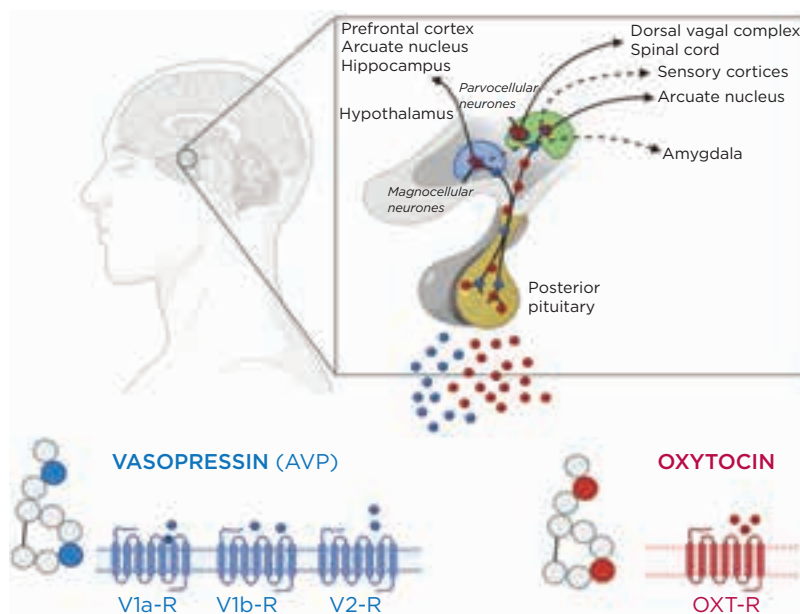
Oxytocin release is controlled by a positive feedback loop, whereby its initial secretion stimulates further production of the hormone. This is essential in pregnancy-related pathways of uterine contraction during birth and lactation, where increases in oxytocin promote stronger responses.

Vasopressin is sometimes referred to as antidiuretic hormone and has two major functions within the body. First, it increases the reabsorption of water into the circulation from kidney tubules. Its secondary role is in the cardiovascular system, through its action on the arterioles, increasing vessel resistance and raising blood pressure.

typical prosocial, empathic and anxiolytic subjective effects. In contrast, in patients, no notable increase was observed, and plasma oxytocin only slightly increased from 60pg/ml (IQR 51–74) by 66pg/ml (IQR 16–94). In agreement with the lack of oxytocin increase, lower MDMA-induced subjective effects such as ‘trustful feelings’, ‘closeness to others’ or ‘happiness’ were observed, reflecting a lack of activation of central key regions important for socio-emotional processing (Figure 2).

Furthermore, in response to MDMA, healthy controls demonstrated reduced recognition of negative emotions (i.e. ‘anger’, ‘fear’ and ‘sadness’) in the emotion recognition task, increased empathy for positive emotions, and reported anxiolytic effects. In contrast, in patients, there was no reduced recognition of ‘fearful’ emotions, no increase in empathy, and no anxiolytic effect. In particular, the lack of increase in ‘positive empathy’ (the ability to share, celebrate and enjoy others’ positive emotions, a state which

Figure 1. Hypothalamic–posterior pituitary axis. Vasopressin and oxytocin are both produced in the hypothalamic supraoptic and paraventricular nuclei, stored and released into the circulation from the posterior pituitary. biorender.com



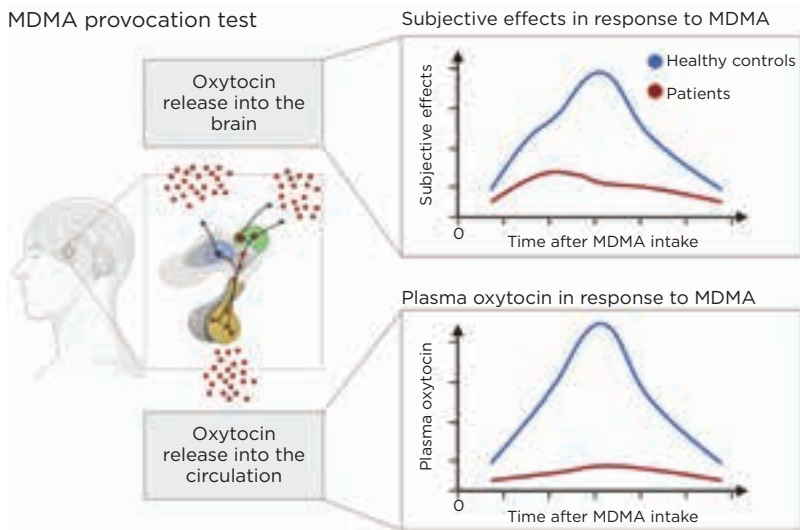


Figure 2. Schematic illustration of the study results.¹⁰ biorender.com

correlates with increased prosocial behaviour, social closeness and well-being) might contribute to the psychological findings observed in the study.

TREATMENT WITH OXYTOCIN?

These results provide strong evidence for a clinically relevant oxytocin deficiency in patients with vasopressin deficiency. This finding opens up new therapeutic possibilities. The effects of oxytocin administration in patients with vasopressin deficiency have only been reported in one small study, demonstrating an improvement in the previously impaired ability to categorise negative emotions after a single dose of intranasal oxytocin.¹¹

Future studies in a larger patient population should investigate the potential therapeutic use of intranasal oxytocin.

The same group at the University Hospital of Basel is currently planning a large study to investigate whether treatment with oxytocin can improve the psychological symptoms in patients with vasopressin deficiency.

CIHAN ATILA
Clinical Scientist

MIRJAM CHRIST-CRAIN
Full Professor in Endocrinology, Co-Head of the Department of Clinical Research and Deputy Head of the Department of Endocrinology

University Hospital Basel, Department of Endocrinology, Diabetes and Metabolism, Department of Clinical Research, Basel, Switzerland

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AN INTERVIEW WITH... REN RENWICK CEO OF THE PITUITARY FOUNDATION



Ren Renwick is Chief Executive Officer of The Pituitary Foundation, a charity offering practical, emotional and peer support to everyone living with or affected by a pituitary condition. Ren has a wealth of experience in the charity sector. Here, she tells us how The Pituitary Foundation works alongside patients, their support networks and healthcare professionals to raise pituitary awareness and reduce time to diagnosis.

What does The Pituitary Foundation do?

We are the UK's patient support group for people living with pituitary conditions of all kinds. At the heart of our work is our range of support services: we have two helplines, one staffed by specialist nurses, and the other by wonderful volunteer pituitary patients. These are free to access and are invaluable to many people. We also run volunteer-led support groups, which provide a forum for people to connect, share experiences and learn

from each other, and we produce print and online resources about living with different pituitary conditions.

Raising awareness is another key part of our work, and we engage with policymakers and the NHS to improve conditions for the pituitary community. Alongside this, we've got a fantastic fundraising programme to help us provide our services – from mountain hikes to marathons, and the

gentler programme of drinks and talks – there is a way for everyone to get involved!

What is most exciting about your job?

The people! Speaking with patients and their families is hugely inspiring. The generosity with which people share their experiences and look to help others is incredible. Our volunteers are brilliant – giving up their time to lead support groups, speak on the helpline and guide and inform our work through committees and boards.

We are very lucky to have wonderful engagement with endocrine professionals who work with us to support the best possible care for patients. It's so exciting to see the research in the area, alongside the incredible care that is provided, day in, day out.

What achievement are you most proud of?

We've recently launched our new website, with a refreshed visual identity and edited content. The team put in a huge amount of work to make the site easy to navigate, so people can find the information they need quickly. We've had great feedback on the site, and are enjoying continuing to develop it.

What are the biggest challenges for the Foundation?

Like any small charity, we have pretty tiny margins, and the financial landscape is challenging. We are reliant on donations as well as grants and sponsorship. We recognise that finances are increasingly tight for everyone – but we know our services are still needed and are committed to keeping the support in place. Our membership scheme is a fantastic way to be part of our community and support our work. It's an affordable yearly amount, and means a lot to us and our activities.

'It's especially important that the next generation of clinicians is engaged in pituitary conditions, and that they specialise to ensure the treatment can continue to be excellent.'

Why is increasing public knowledge so important?

If more people knew about pituitary conditions it could help reduce the time to diagnosis, which would be hugely beneficial. The trauma of a delayed diagnosis can have a lasting impact, on top of the management of a condition. I'd love more people to understand the effect that different pituitary conditions can have and how people living with conditions can be supported.

October marks Pituitary Awareness Month, and this year's theme is 'Spotlight on prolactin'. We will be raising awareness of prolactin and

prolactinoma. Throughout the month, we'll host information events and support groups, and share resources around the subject.

'We need to look to the future and ensure that the next generation of pituitary patients receives the best care possible.'

I'd also love it if every single person diagnosed with a condition knew about our services. We reach and support thousands of people each year, but there is still work to do in making sure we are available and accessible to everyone.

What more is needed to educate clinicians about pituitary conditions?

The Society for Endocrinology has brilliant meetings, which enable clinicians to share new research and insights into the field. It's especially important that the next generation of clinicians is engaged in pituitary conditions, and that they specialise to ensure the treatment can continue to be excellent.

We also know that there are issues with awareness amongst general ward, A&E and primary care staff. There are some great developments which really help patients, like the introduction of the Steroid Emergency Card and the renaming of AVP deficiency (diabetes insipidus). We do a lot of work around raising awareness amongst different clinical groups, and are hoping to create a new GP training module on pituitary conditions.

I'd love every clinician to know about our services and to signpost them for all of their patients.

What are your key aims over the next few years?

We've got so much to do! We've agreed a really ambitious strategy which drives forward the support to people living with conditions. But we recognise that, post-pandemic, we're working alongside a health service that's under unprecedented pressure. We also know that the needs of patients are changing, and mental health increasingly needs to be addressed. We want to see support evolving to address these changing needs, while remaining of the highest quality.

We've also recognised that we need to look to the future and ensure that the next generation of pituitary patients receives the best care and diagnosis possible. We need to consider how technological advances can support this, and what the relationship with the NHS will be like under successive governments.

I'm excited for the future – we have a great team of staff, as well as clinicians who give their time and expertise in spades, incredible volunteers and inspiring, generous-spirited patients. Everything is possible!

RETURNING THIS SUMMER

Series 3 of our award-winning podcast!

HORMONES

THE INSIDE STORY

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“ Interesting and **really useful information.** So worth listening to!

“ Fantastic, **really insightful** and interesting science podcast.

“ Well researched and well presented podcast that makes the subject of hormones **accessible to a wide audience.** Highly recommended!

“ **Really love this podcast** – interesting stories and guests, sounds great and nice to hear the science of hormones covered in a sensible but fun way. Thank you!

“ I'm really enjoying this this podcast – **perfectly pitched.** I'm learning a lot and finding the episodes really absorbing.

All reviews 5 star from Apple Podcasts

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Shape your magazine

JOIN *THE ENDOCRINOLOGIST* EDITORIAL BOARD

Do you want to keep the Society's members informed about the key issues affecting our discipline? Then why not apply to join the Editorial Board for your Society's member magazine: *The Endocrinologist*?

The Endocrinologist provides a vital line of communication between members, helping to foster a sense of community and loyalty. Editorial Board members create and commission content for *The Endocrinologist*, helping to produce a publication that highlights news and issues that affect clinicians, scientists and nurses working in endocrinology, at all career stages.

WHAT YOU'LL GET TO DO...

As an Editorial Board member, you'll maintain an overview of the magazine's content, to ensure that it represents members' interests and is in line with the Society's aims. This includes:

- identifying and commissioning articles from authors
- reviewing all material to decide on its suitability in terms of subject, interest, quality and topic
- writing 'hot topics' from the latest journal articles
- working with the Society team to ensure that the production schedule runs smoothly
- attending four Editorial Board meetings per year (no more than one is in-person).

'MEET NEW PEOPLE, TRY NEW THINGS AND FLEX YOUR CREATIVE MUSCLES'

Read on to hear from current Editorial Board members about how they got involved and why you should apply to be part of *The Endocrinologist* team!

LOUISE HUNTER

Louise is a Clinical Senior Lecturer in Endocrinology at the University of Manchester. As well as being a member of the Editorial Board, she has been selected as one of the Society's 2023 Leadership and Development Programme Awardees.

How did you first get involved with the Society?

During my FY2 year, my rotation took me to the Paediatric Endocrinology Department at Yorkhill Hospital in Glasgow. The consultant team there really nurtured my interest in endocrinology, and encouraged me to become a member of the Society. I benefited early on from one of the award schemes that funded attendance of the SfE BES conference – that lured me in!

What do you enjoy most about being part of *The Endocrinologist* team?

Working with the rest of the Editorial Board is brilliant – they're a lovely bunch of people. I like the brainstorming sessions when we plan an issue, and seeing the final version come together is very satisfying.

How has serving on the Editorial Board helped your career?

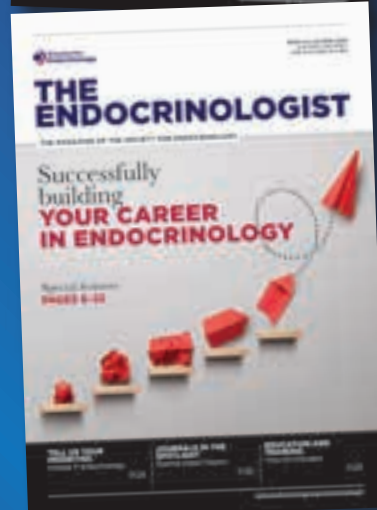
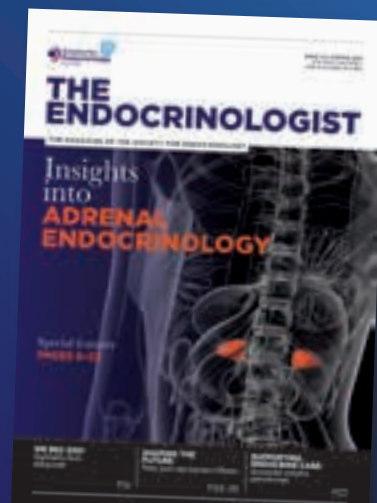
We get to read all the features as each issue is being put together. This is both educational and a great means of finding out who the experts are in each field.

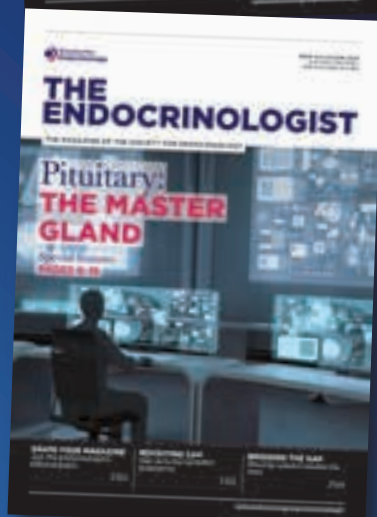
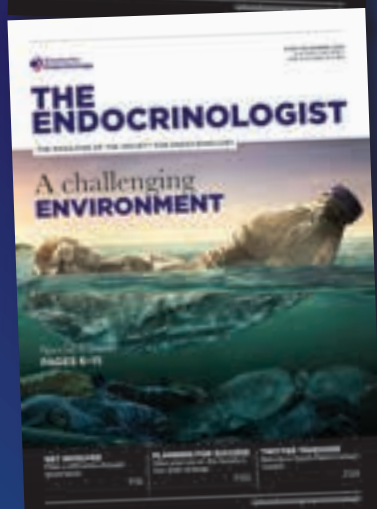
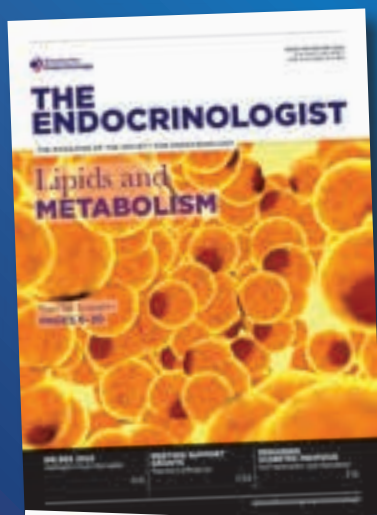
Which feature in *The Endocrinologist* stands out to you?

There's not a single feature, but there are some issues I'm particularly pleased with. I think it's important that *The Endocrinologist* is a source of inspiration and advice for early career members and, as such, the recent career-focused issues (Autumn 2022, Autumn 2019) are standouts for me. I hope readers found them useful. As part of the Centre for Biological Timing at the University of Manchester, I'm biased, but I think our Winter 2019 issue (Rhythms of Life: Timing in Endocrinology) was especially interesting!

Why should someone join the Editorial Board?

It broadens your perspective on the field, and it gives you the opportunity to shape discussion on topical issues. The time commitment isn't significant – we meet (usually virtually) a few times a year, with most business conducted via email.





CRAIG DOIG

Craig is an Associate Professor in Metabolism at Nottingham Trent University. In addition to being an Editorial Board member, he sits on the Society's Science Committee, and is part of the SfE BES Programme Committee.



How did you first get involved with the Society?

As a postdoc in Birmingham, maybe in 2012?! It was a great place of endocrine excellence. I went to my first SfE BES conference (in Harrogate of course). I was very taken with how friendly everyone was, the science being done, and the strong feeling of community.

What do you enjoy most about being part of *The Endocrinologist* team?

Oh, without a doubt, it's meeting with my colleagues on the Editorial Board. They're a delight to hang out with and we have great fun brainstorming! Also, producing a tangible object every quarter is satisfying. Academia is packed with opportunities for bureaucracy, forms get completed and sent, you can't be sure they ever get read. But, with *The Endocrinologist*, we get to create a product every 12 weeks, and it's read too ... I hope.

How has serving on the Editorial Board helped your career?

The dull answer to this is that it ticks a box on the CV. The correct and better answer is that it has been a wonderful experience to meet new people, try new things and flex my creative muscles. Endocrinology is a field that occasionally allows us to create an issue slightly on the edge of the remit. It doesn't always make the path easy ... and we have a very, very patient Managing Editor!

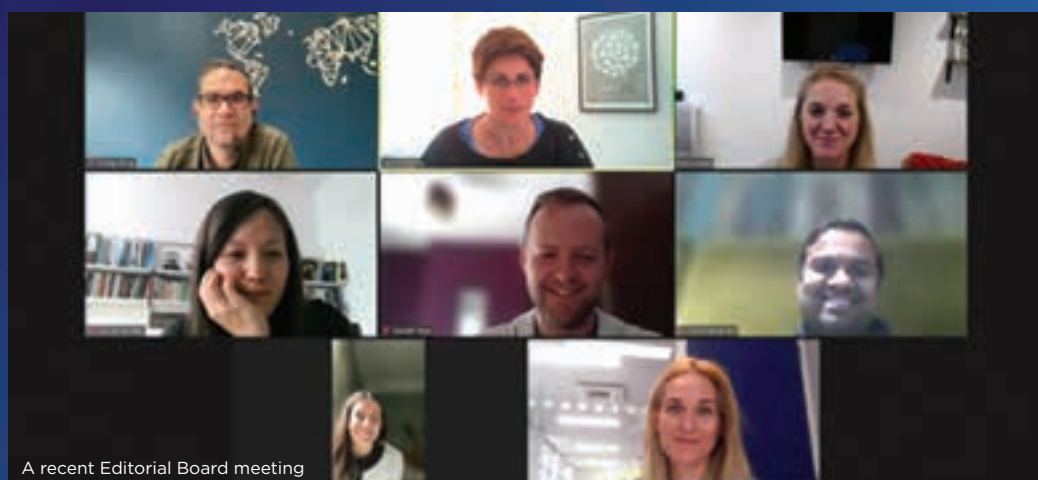
Which job in the role of Editorial Board member stands out to you?

It's really the consistency and the sum of all the jobs needed to create an issue that stand out. Generating hot topics, writing and commissioning articles, even coming up with ideas for cover images: there's a huge variety in the role – it's exciting.

Why should someone join the Editorial Board?

It's enjoyable, and it's also a career development opportunity. I've learned so much from those I've worked with on the Board. The Editors in particular (shout out to Helen Simpson and Kim Jonas) have been great sources of inspiration. For example, their creativity and pragmatism dealing with difficult issues have been wonderful to see. As a result of being on the Editorial Board, I've made new contacts and gained new knowledge about areas of endocrinology that I'm not normally exposed to. That box on the CV has been ticked too!

The application deadline is **Wednesday 4 October**
Apply online at www.endocrinology.org/editorialboard/apply



A recent Editorial Board meeting

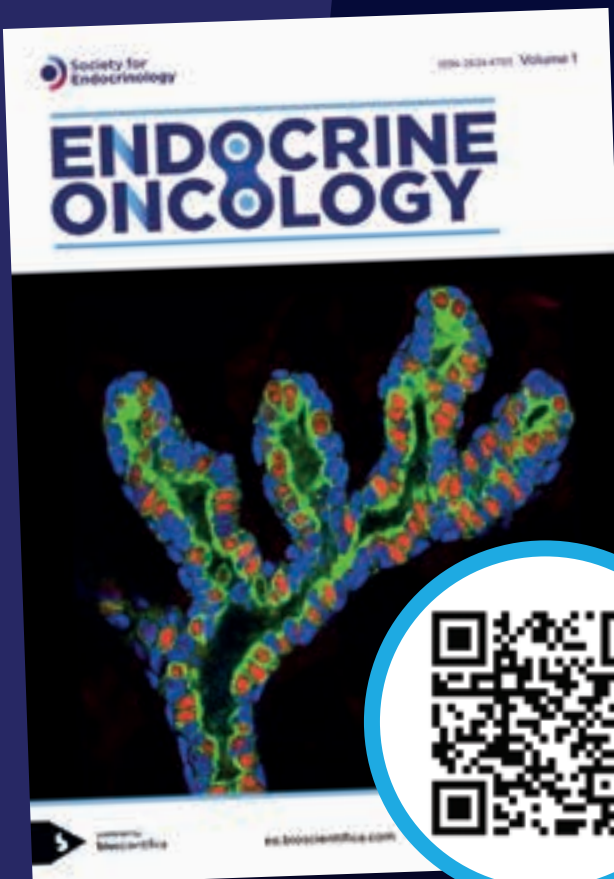
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Read Editor-in-Chief, Justo P Castaño's editorial about the “**birth and growth of *Endocrine Oncology***”

“As scientists, the search for suitable visibility is a primary goal. We are required by the research community, funding bodies and society at large to find the right platform to reach our optimal target audience of colleagues and peers: those with whom we must share, discuss and leverage the results from our research and, ultimately, bring it closer to patients.”

Professor Justo P Castaño



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CaHASE2 – call for participants

REVISITING HEALTH STATUS IN CONGENITAL ADRENAL HYPERPLASIA

Congenital adrenal hyperplasia (CAH) is one of the commonest forms of primary adrenal insufficiency, with an incidence of about 1 in 10,000 to 1 in 15,000. The Congenital Adrenal Hyperplasia Adult Study Executive (CaHASE), supported by the Society for Endocrinology, was formed 20 years ago to study the health status of patients with CAH in adulthood. It is now more than a decade since several studies highlighted the suboptimal health status and care provision among adults with CAH, which were associated with significant co-morbidities at a relatively young age.^{1–3}

CaHASE has become the landmark global study providing information on the health status in adults with CAH.¹ The poor health outcomes that were identified by CaHASE were a driver for a new modified release formulation of hydrocortisone that was developed in the UK.⁴ The CaHASE study also underpinned the development of the I-CAH registry (<https://home.i-cah.org>) that has resulted in several important insights into CAH around the world.

The key findings of CaHASE can be summarised as follows:¹

- Only a minority of adults living with CAH in the UK were under specialist endocrine care.
- Glucocorticoid replacement was generally non-physiological.
- Androgen levels were poorly controlled.
- Patients had adverse metabolic profiles.
- People with CAH showed increased rates of osteoporosis.
- Patients were found to have impaired fertility.
- People with CAH had a reduced quality of life.

Similar findings were reported in a study at the National Institutes of Health² and in a French cohort study.³ Evidence suggested that poor health outcomes related to treatment rather than genotype.⁵

TIME FOR AN UPDATE

Considering that recruitment into CaHASE took place in 2003–2007, the data from this study reflect the situation in the UK some 15–20 years ago. In the early 2000s, CAH clinical guidelines^{6,7} were widely publicised that suggested changes in the use and dosage of corticosteroid replacement in CAH in all age groups. Thus, there is now a generation of young adults with CAH who should have presumably been treated differently during childhood and adolescence than the cohorts who were investigated in the early to mid-2000s.

However, a recent study in children and young people from the UK demonstrates an increased prevalence of problems with growth and weight gain in children with CAH, and suggests reduced quality of life during paediatric care.^{8,9} Furthermore, a recent international study performed by I-CAH, in combination with members of CaHASE and Endo-ERN, has reported considerable variation in the management of adults with CAH.¹⁰

The Society for Endocrinology performed a survey of its members this year, and this has also confirmed variation in clinical care provision among adults with CAH in the UK and Ireland. The majority of respondents managed patients with CAH in general endocrinology clinics. Patients were most commonly seen six-monthly or yearly by different centres, and marked variation was reported with regards to biomarkers that were used for CAH monitoring, including the use of markers that are not commonly recommended by guidelines.¹¹ There was no consensus on the optimal timing for monitoring biochemistry in relation to corticosteroid replacement. A quarter of respondents in specialist clinics used the I-CAH registry and a third of those in general clinics were unaware of this platform.

‘A recent study in children and young people from the UK demonstrates an increased prevalence of problems with growth and weight gain in children with CAH, and suggests reduced quality of life during paediatric care.’

CaHASE2: A NEW PROGRAMME

We have therefore developed a programme of work:

- to reassess the clinical management and health status of adults living with CAH in the UK and Ireland, 20 years after the first CaHASE study
- to implement a strategy for prospective continuous recruitment with longitudinal data collection in I-CAH
- to identify specific unmet needs, through standardised, deep clinical phenotyping across all participating centres.

The longitudinal data collection will start in November 2023, and 21 centres have already signed up to participate in the study. If you are interested in participating in CaHASE2, please contact the Society for Endocrinology at clinical@endocrinology.org.

CaHASE2 STEERING GROUP

Nils Krone (Chair), Faisal Ahmed, Sue Elford, Yasir Elhassan, Lynette James, Sofia Llahana, Michael O'Reilly, Aled Rees, Jeremy Tomlinson

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Bridging ‘the valley of death’ THE CRUCIAL ROLE OF CORPORATE LIAISON



The divide that has emerged between cutting edge laboratory research and the patient seeking help in clinic has been described as ‘the valley of death’. This is a place where promising discovery science goes when it fails to benefit patients. As a clinical academic, I feel my *raison d'être* is translational research, and I've recently joined the Society's Corporate Liaison Committee. I'm hoping that this will help me define the problems in this space and identify solutions.

A TIME OF CHANGE

Traditionally, it was seen as a badge of honour for a university-based academic to work independently from industry. Pharmaceutical companies did not generate trust or exhibit transparency. More recently, the collaborative development of COVID vaccinations has demonstrated the power of academia and industry working towards a common purpose, and views are shifting.

Effective collaboration between researchers and industry is essential to ensure discoveries benefit society. ©Shutterstock



In academia, the days of lauding the brilliant scientist working in isolation in the laboratory are coming to an end. No scientific discovery will disrupt and transform medicine if it does not leave the laboratory, and this is starting to be reflected in promotion criteria and research excellence frameworks. For the life sciences sector, transparency, reliability and trust are key for improving health and also make good business sense. It's time for open innovation models, entrepreneurship and transparency to improve the lives of patients.

ADDRESSING THE CHALLENGES

Cross-sector working can be fraught with difficulty; motivations, language and culture can vary widely across sectors. Skills are required to navigate different timescales and resources, to break down traditional mindsets and to establish common goals. This is not part of routine university or clinical training programmes, but is essential for driving improvements in healthcare.

The Society of Endocrinology Corporate Liaison Committee is working to increase understanding between sectors, and to provide opportunities for members to interact across the life sciences, in order to influence policy and facilitate joint partnerships for the benefit of patients.

Membership of this Committee has taken me outside my comfort zone and is developing my leadership skills to make science have real impact in society. We all need to learn to collaborate effectively and assess problems from different angles to really translate our science for human application. Perhaps then we can reclaim the wasteland between science and medicine and facilitate translation for collective benefit.

You can find out more about the work of the Corporate Liaison Committee at www.endocrinology.org/corporate-liaison-committee.

JACQUELINE MAYBIN

Reader and Honorary Consultant Gynaecologist, MRC Centre for Reproductive Health, University of Edinburgh

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SUMMER 2023 CONFERENCE ROUND-UP

We asked Society members to share their thoughts and highlights from two major endocrinology conferences this summer: ECE 2023, organised by the European Society of Endocrinology (ESE), and ENDO 2023, the annual meeting of the Endocrine Society.

ECE 2023

The 25th European Congress of Endocrinology took place in Istanbul, Turkey on 13–16 May. Here, Society members Cynthia Andoniadou and Helen Simpson give us their insights.

CYNTHIA ANDONIADOU

Reader in Stem Cell Biology and Associate Dean for Postgraduate Research, King's College London

I had a superb experience at ECE 2023 but, as Chair of the ESE Congress Committee, I am somewhat biased in my opinion of the programme!

As a basic scientist working on stem cells of the hypothalamus–pituitary–adrenal axis, I found that there were sufficient basic and translational talks to attract me for this content alone, despite ECE being a mostly clinical conference. At the same time, I valued keeping informed about the clinical advances in my field, and networking with colleagues from Europe and beyond.

On site, I attended all the plenaries, pituitary and neuroendocrinology sessions and adrenal and cardiovascular sessions. Even just through the (truly stellar) plenaries, I received a very well-rounded experience. The six plenary sessions and seven award lectures covered a broad range of topics across varied endocrinology focus areas. I have been able to watch most of the remaining Congress content through ECE@Home (ESE's on-demand catch-up service), although I still have a few talks to go!

Within the pituitary and neuroendocrinology symposia content, highlights for me were 'Spotlight on the posterior pituitary' (Chris Thompson, Cihan Atila and Alessandro Peri) as well as 'Prolactinomas' (Erika Peverelli, Gerald Raverot and Renata Auriemma). Both were extremely well attended. Among the adrenal and cardiovascular content, I particularly enjoyed the symposium on 'Aberrant/illicit expression of receptors in adrenal lesions' (André Lacroix, Peter Kamenicky and Hervé Lefebvre) and the basic symposium on 'Research advances in adrenocortical carcinoma (ACC)

pathogenesis' (Katie Basham, Pierre Val and Andreas Schedl). The speakers in this session presented recent cutting edge findings that reveal valuable new insights into the molecular underpinnings of ACC.

Excellent basic science also featured in the New Scientific Approaches sessions:

- *Thyroid effects on organoids* – Sylvie Remaud-Jachiet
- *Single cell -omics* – Igor Adameyko
- *Circulating DNA to identify targetable mutations in metastatic endocrine cancers* – Rodrigo Toledo.

These sessions, given by world experts, are always superb and approachable for all audiences, so I would highly recommend catching some of them next year.

HELEN SIMPSON

Consultant Endocrinologist, University College London Hospitals

This was my first ECE and I went to deliver my first international invited speaker talk. It was also my first overseas meeting for many years: single parenting and a pandemic don't lend themselves to globe trotting. Flying in over the Bosphorus made me aware of the geographical location, bridging Europe and Asia. Coupled with the fact that Turkey's general election happened whilst we were there, my attention was acutely drawn to the geopolitics.

Once at the meeting, the sessions I enjoyed most included the symposium 'Spotlight on the posterior pituitary' and a rapid communications session on adrenal insufficiency.

I loved hearing Chris Thompson distil years of clinical experience into 30 minutes; take aways for me were the use of a visual analogue scale for thirst to document adipsia, and being reminded of the data for measuring co-peptin with hypertonic saline to diagnose cranial diabetes insipidus/ vasopressin (AVP) deficiency. As an aside, the debate on the renaming of cranial diabetes insipidus concluded that the audience did not favour using the new name AVP deficiency, which was provocative!



The welcome reception at ECE 2023. ©Cynthia Andoniadou



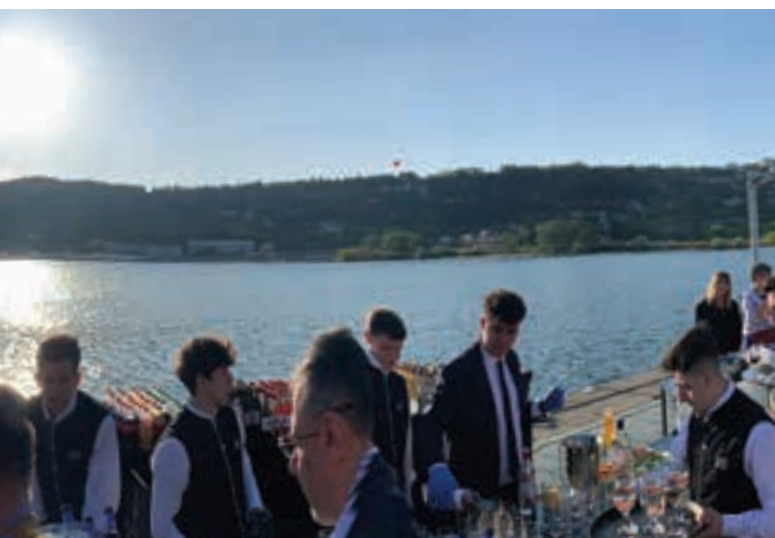


Maria Fleseriu and Helen Simpson at ECE 2023. ©Rob Fowkes

I really enjoyed the rapid communications session: three-minute presentations by research fellows and trainees, followed by an oral poster session which gave the opportunity to talk about their work in more detail. I loved the enthusiasm and passion they had for their work, and also felt encouraged, as the consensus was that it is hard to know who is at risk of adrenal crisis.

Whilst it was great to see people (as demonstrated above by Maria Fleseriu and me deciding who will be chief physician; photo credit to Rob Fowkes), the expense and time out of work present a challenge, and travel with its impact on climate change deserves thought. It was great to see hybrid sessions and the ability to see sessions on demand, which has many benefits, not least increased inclusion.

And how did my talk go? Well, I'm not best to comment on that, but there was a long queue of people asking questions and a request for more sessions on transition at future meetings. I'll see what I can arrange.



ENDO 2023

The 2023 Annual Meeting of the Endocrine Society was held on 15–18 June in Chicago, IL, USA. Here are some highlights from Kate Laycock and Sophie Clarke.

KATE LAYCOCK

Endocrinology Registrar, Queen Mary University of London, William Harvey Heart Centre



As a first-time attendee and presenter at ENDO 2023, I was struck by the size of this vast conference. However, whatever ENDO might have lacked in intimacy, it made up for in its breadth and quality. At any one time, multiple sessions were taking place on key areas of endocrinology. I was delighted to see presentations on a lot of unpublished, or very recently published, work.

I presented some of my data on adrenal single cell sequencing to experts from different countries, and found ENDO 2023 particularly notable for the presence of global lecturers and attendees. The conference delivered a series of Meet the Professor sessions by international speakers that were accessible to trainees, as well as social events directed at early career members.

I particularly enjoyed the Meet the Professor session entitled 'How do I work up a woman with androgen excess?' and the Adrenal Tumor Board event 'Selected cases from the adrenal clinic'.

SOPHIE CLARKE

Consultant Endocrinologist, University College London Hospitals



Due to the pandemic and home and work commitments, I had not attended ENDO for several years. I had forgotten the vast scale that it operates on, and how many high quality sessions it includes.

As a reproductive endocrinologist, some key highlights for me included attending the session on the new international guidelines for polycystic ovary syndrome, as well as the session reporting the findings of the TRAVERSE trial, which sought to examine the cardiovascular safety of testosterone treatment in hypogonadal men at risk of cardiovascular disease.

I also had the privilege of being invited to take part in a symposium on long COVID, where I presented work on the impact of COVID-19 on the hypothalamic–pituitary–adrenal and –thyroid endocrine axes in those with persistent symptoms. It was fascinating to meet other contributors to the field, and to learn of ongoing research in the area. I was also able to present work from a clinic I undertake with the Paediatric Adolescent Gynaecology Team, investigating the most effective hormonal therapies to achieve menstrual suppression for those patients who require it preoperatively. It was great to hear of others' experience, both from the USA and from other international centres.

As well as being able to find out about the latest research, ENDO 2023 provided a great chance to catch up with friends and meet others working in similar fields and – in the midst of the challenges we currently face in the NHS – a great chance to remember all that is fun and brilliant about endocrinology.